Notice of Allowability	Application No.	Applicant(s)	
	10/683,576	VATNER ET AL.	
	Examiner	Art Unit	
	Robert B. Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *RCE filed July 24, 2006*.

2. ☒ The allowed claim(s) is/are *34-50*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Ms. Christine E. Dietzel on August 9, 2006.

The application has been amended as follows:

Please replace paragraph [0028] of the specification, on page 11, lines 15 through page 12, line 2 with the following new paragraph [0028]:

[0028] FIGURE 6A, 6B, 6C, 6D, 6E and 6F depicts analyses of Tg-DN-Mst1 or non-transgenic control (nTg) mice. In (A) three transgenic lines, #9, #10 and #11, are probed for Mst1 expression in the heart. In (B) Immunoblot analyses of the heart homogenates with anti-myc antibody. In (C)-(F), Tg-DN-Mst1 or non-transgenic control mice (NTg) were subjected to 20 min ischemia and 24h reperfusion or sham operation. (C) The heart homogenates (100 μg) obtained from ischemic (I) and non-ischemic (N) areas of the left ventricle (LV) or from intact LV of the sham operated mice were subjected to in gel myelin basic protein (MBP) kinase assays. Ischemia/reperfusion (I/R) increased kinase activities of Mst1 in the ischemic area of NTg mice, while activation of Mst1 by I/R was completely abolished in Tg-DN-Mst1. (D) The effect of I/R upon the extent of LV myocardial infarction (MI) in Tg-DN-Mst1 and NTg control mice. The MI area/area at risk (AAR) was determined as described in the Method section. Note that

MI area/AAR was significantly smaller in Tg-DN-Mst1 compared with that in NTg. (E) LV tissue sections were subjected to TUNEL staining and DAPI staining. n=11. (F) Genomic DNA was isolated from non-ischemic (N) and ischemic (I) areas and DNA laddering assays were performed. The extent of DNA laddering in response to I/R was significantly smaller in Tg-DN-Mst1 compared with that in NTg. n=3.

Claim 34 (Presently amended) A method of treating cardiac disease in a mammal comprising administering to ~~or expressing in~~ said mammal an effective amount of a compound or agent that blocks or otherwise specifically inhibits mammalian Ste20-like kinase (Mst1) wherein said compound is an Mst1 inhibitor which is a dominant negative mutant of Mst1.

Claim 38 (Presently amended) A method of modulating cardiac myocyte apoptosis in a mammal comprising administering to ~~or expressing in~~ said mammal an effective amount of a compound or agent that blocks or otherwise specifically inhibits mammalian Ste20-like kinase (Mst1) ~~Mst1~~ wherein said compound is an Mst1 inhibitor which is a dominant negative mutant of Mst1.

Claim 40 (Presently amended) A method of reducing cardiomyopathy in a mammal comprising administering to ~~or expressing in~~ said mammal an effective amount of a compound or agent that blocks or otherwise specifically inhibits mammalian Ste20-like kinase (Mst1) wherein said compound is an Mst1 inhibitor which is a dominant negative mutant of Mst1.

Claim 42 (Presently amended) A method for treating cardiac disease in a mammal comprising administering to ~~or expressing in~~ said mammal an effective amount

of a compound or agent that blocks or otherwise specifically inhibits mammalian Ste20-like kinase (Mst1) wherein said compound is an Mst1 inhibitor which is a dominant negative mutant of Mst1, in combination with one or more other compounds for treatment of cardiac disease or of atherosclerosis.

Claim 45 (Presently amended) A method for reducing the risk of cardiomyopathy or cardiac dysfunction in a mammal wherein said mammal has suffered a myocardial infarct or other coronary event wherein blood flow to the heart is reduced comprising administering to ~~or expressing in~~ said mammal an effective amount of a compound or agent that blocks or otherwise specifically inhibits mammalian Ste20-like kinase (Mst1) wherein said compound is an Mst1 inhibitor which is a dominant negative mutant of Mst1.

Claim 47 (Presently amended) A method of cardioprotection in a mammal, wherein a specific inhibitor of Mst1 ~~selected from~~ is a dominant negative mutant of mammalian Ste20-like kinase (Mst1) ~~Mst1~~ and is administered to ~~or expressed in~~ said mammal in conjunction with or following therapy with a compound or drug which is cardiotoxic.

Reasons for allowance

The following is an examiner's statement of reasons for allowance: The method of the invention which comprises the administering of a dominant negative mutant of

mammalian Ste20-like kinase (Mst1) that specifically blocks or inhibits MST1 has been determined to be novel over the prior art.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B. Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert B. Mondesi

8-9-06

JON WEBER
SUPERVISORY PATENT EXAMINER